REMARKS/ARGUMENTS

Reexamination and reconsideration of this application, withdrawal of the rejections, and formal notification of the allowability of all claims as now presented are earnestly solicited in light of the remarks that follow.

Claims 1-4 are pending in the application. Claims 1, 3, and 4 have been amended herein. Claim 1 has been amended to recite that the claimed compound is heterobifunctional. Support for this amendment may be found throughout the specification, such as on page 8, which includes the definition of heterobifunctional. Claim 3 has been amended to harmonize the list of W linkages with the list appearing in paragraph 38 on page 9 of the specification. Claim 4 has been amended to adjust the list of Q moieties to match the list on page 10, paragraph 42. It is respectfully submitted that no new matter is introduced by these amendments.

Claims 3 and 4 stand rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. In particular, the Examiner has objected to the terms "esters" and "disulfides" in claim 3 and the terms "active esters" and "active carbonate" in claim 4. As noted above, Applicants have amended claims 3 and 4 to match the exemplary W and Q moieties set forth in the specification. As a result, Applicants respectfully request reconsideration and withdrawal of this rejection.

Claims 1-4 are provisionally rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over the claims of copending Patent Application No. 10/684,946. In response, Applicants submit herein a Terminal Disclaimer. In light of the Terminal Disclaimer, Applicants respectfully request reconsideration and withdrawal of this rejection.

Claims 1-4 stand rejected under 35 U.S.C. §103(a) as being unpatentable over the Yang reference in view of U.S. Patent No. 5,840,900 to Greenwald *et al.*, and if necessary, in further view of U.S. Patent No. 5,977,277 to Yokoyama *et al.* The Examiner alleges that the Yang reference discloses a heterobifuntional PEG molecule having an acrylate group on one terminus, and relies upon the Greenwald reference as disclosing a prodrug composition containing a hydrolyzable linkage. The Examiner concludes that it would have been obvious to provide a hydrolyzable linkage in the backbone of the PEG molecule of the Yang reference in order to enable releasing of a biologically active moiety. The Examiner further notes that the Yokoyama reference discloses a heterobifunctional PEG having an acrylate group on one terminus. Applicants respectfully traverse this rejection.

The Yang reference is directed to a study of enzymes modified by heterobifunctional PEG molecules containing an acrylate end group. In the introduction section, the reference notes that it is important to develop enzyme compositions that are stable in non-conventional environments, such as non-aqueous solvents. Thus, the goal of the study is to produce "solvent-stable enzymes" by modification of an enzyme with a heterobifunctional PEG molecule. The reference goes on to tout the stability of the resulting polymer molecules in both aqueous solution and organic solvents, stressing that polymeric crosslinking and the strong binding between the protein molecules and the polyacrylate backbone are important factors that provide molecule stability (see page 4846, second column). Even the relatively harsh methanol rinse test described in the Yang reference confirmed the stability of the PEG-enzyme biopolymer. Thus, it is clear that the overwhelming focus of the reference is on the development of PEG-enzyme polymer systems that enable enzymes to remain active and stable in aqueous and organic media. There is no mention of the desirability of utilizing polymer structures deliberately designed to break down in a solvent system.

The Greenwald patent is directed to prodrug compositions that contain PEG polymers linked to a drug moiety, wherein the linkage is designed to hydrolyze *in vivo*. The Greenwald reference teaches that the hydrolyzable linkage between a polymer and a parent drug compound can degrade at a rate that allows a sufficient amount of the parent molecule to be released *in vivo* before clearance of the prodrug from the plasma or body.

There is simply nothing to suggest to one of ordinary skill in the art to incorporate the hydrolyzable linkage teaching in Greenwald with the Yang reference. The Yang reference is directed to polymer systems that are intentionally developed in order to retain stability in a variety of media, including aqueous systems and organic solvents. One of skill in the art would readily recognize that the use of a hydrolyzable linkage in the polymer backbone would be detrimental to the express goals of the Yang reference. The Yang reference clearly teaches away from the use of unstable linkages in the molecules described therein. When molecular stability is expressly sought, one of ordinary skill in the art would be disinclined to utilize hydrolyzable linkages.

The express teaching away of Yang obviously reduces any value of the Yokoyama patent in the rejection as well. However, it is further noted that the Yokoyama reference is directed to a completely different field of use than either Yang or Greenwald. Specifically, the Yokoyama patent is directed to the use of polymer systems as liquid electrolytes in an electrochemical element. There is no mention in Yokoyama of binding of a polymer to a biologically active substance, such as an enzyme or drug molecule. One of ordinary skill in the field of art described in the Yang reference would not look to the Yokoyama patent for potential modifications of the system described in Yang.

Further, it is noted that claim 1 has been clarified to recite a heterobifunctional compound. Contrary to statements made by the Examiner, the Yokoyama reference does not disclose heterobifunctional compounds. The Examiner's attention is directed to Formulas I to IV, wherein four structures of PEG polymers are provided. Formulas II and IV are obviously homobifunctional molecules. Formula III describes a molecule having an acrylate end group and a non-reactive alkoxy end group. Formula I, which is illustrated incorrectly in the Abstract, is also directed to bifunctional compounds wherein one end group is a non-reactive alkoxy group (see column 2, lines 25-36). Thus, none of the polymer structures set forth in the Yokoyama patent is directed to a heterobifunctional PEG molecule having an acrylate group on one terminus and a different reactive functional group on a second terminus.

In light of the foregoing, Applicants respectfully request reconsideration and withdrawal of this rejection.

Consideration of Previously Submitted Information Disclosure Statement

The Examiner has indicated that reference cite numbers 20 and 21 of Form PTO-1449, that was submitted with Applicants' Information Disclosure Statement filed August 17, 2004, are not in the record. Applicants enclose a copy of the stamped postcard indicating that the Office received the two references. However, in order to expedite consideration of the references, an additional copy of each reference is enclosed along with another copy of Form PTO-1449. Accordingly, it is requested that an initialed copy of Form PTO-1449 be forwarded to the undersigned with the next communication from the PTO.

It is believed that all pending claims are now in condition for immediate allowance. It is requested that the Examiner telephone the undersigned should the Examiner have any comments or suggestions in order to expedite examination of this case.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR §1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,

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